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COUNTRY AND INTERCOUNTRY PROGRAMMES AND PROJECTS

PROJECT RECOMMENDATION OF THE ADMINISTRATOR

Assistance for a global project

Special Programme for Research and Training in Tropical Diseases (Phase II) (GLO/80/005)

Estimated UNDP contribution:	$7,567,300
Duration:	Four years
Executing Agency:	The World Bank will act as fiscal agent and the World Health Organization (WHO) will be responsible for the implementation of project activities

I. Background

1. At its January 1978 meetings (E/1978/53/Rev.1, ANNEX II, para. 6), the Governing Council approved a contribution of $5.5 million for the Special Programme for Research and Training in Tropical Diseases (TDR), of which UNDP is a co-sponsor together with WHO and the World Bank. 1/ This contribution followed preparatory assistance 2/ in the amount of $107,500 which the Council approved at its twenty-second session in June 1976 (E/5846/Rev. 1, para. 298), bringing the total amount thus far contributed by UNDP to the Programme to $5,607,500. The Programme has two broad objectives, namely: (a) promotion and support of research aimed at developing new and improved tools for the prevention, diagnosis and treatment of

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1/ DP/PROJECTS/R.9/Add.4.

2/ DP/PROJECTS/R.6/Add.1.

* This document will be derestricted upon approval of the project. See document DP/526, which will be issued in June 1981.

six major tropical diseases; and (b) strengthening of national institutions, including training, for the purpose of increasing the research capabilities of the developing countries affected by the diseases. The six diseases included within the purview of the Programme are: malaria, schistosomiasis, filariasis, trypanosomiasis (both African Sleeping sickness and Chagas' disease), leishmaniasis and leprosy. Together, these diseases affect hundreds of millions of persons in Africa, Asia and Latin America, at enormous cost in terms of human well-being and economic productivity.

2. The Programme is now in full swing, and has elicited impressive support from the international donor community, as well as from research institutions and individual scientists around the world. During the year 1980 22 Governments and organizations co-operating with the Programme contributed $22.7 million towards its support, for a total of $70.6 million contributed since the Programme's inception. The UNDP Regional Bureaux for Africa and for Asia and the Pacific are contributing to the trypanosomiasis and malaria components of the Programme. Extensive links with the world scientific community have been established and continue to be expanded. The Programme is now in communication with some 10,000 scientists and institutions. Of these, approximately 4,300 are in the developing endemic countries. The Programme also collaborates with the pharmaceutical industry in research and development towards production and field application of new drugs, vaccines and diagnostic tests. To date, over 40 scientists from industry have participated in TDR activities and more than 70 collaborative projects with the pharmaceutical sector have been completed or are under way. The Programme is also collaborating closely with the Food and Agriculture Organization of the United Nations (FAO) and the United Nations Environment Programme (UNEP) with respect to certain activities, as well as with a number of centres and programmes supported by UNDP, namely, the International Laboratory for Research on Animal Diseases, the International Centre for Insect Physiology and Ecology and the Onchocerciasis Control Programme in the Volta River Basin Area. Co-operation has also been established with the Rockefeller Foundation and the Walter Reed Army Institute of Research.

3. The Programme is revieved and evaluated through the mechanisms of the Joint Co-ordinating Board, the Standing Committee, and the Scientific and Technical Advisory Committee, which have been established by the co-sponsors and the Co-operating Parties. These mechanisms are described in a Memorandum of Understanding endorsed initially by representatives of 32 Governments and the three co-sponsoring Agencies. At the p resent time, 72 WHO member countries take part in the TDR Programme, and the participation of the Governments of all Members and their institutions and scientists is promoted. It is clear from the above that the Programme has achieved truly global status, and has evoked wide interest and support among both developed and developing countries. The activities of the Programme are planned and managed by multidisciplinary groups of national scientists organized into Scientific Working Groups, each with clearly defined goals. Such Groups have been organized for each of the six diseases, and four trans-disease Programme Components. A Research Strengthening Group guides the training and institution strengthening activities.

II. The project

4. From its inception until the end of 1979 the Programme has supported a total of 804 projects, of which 602 were in the Research and Development Programme Area, and 202 in the Research Capability Strengthening Area. Of the latter, 165 were in support of training, and 37 for institution strengthening. Since 1975 more than $34 million has been obligated for direct project support, 70 per cent of which has been for research and development activities and 30 per cent for research capability strengthening. Intensive efforts have been made to involve institutions and scientists from the developing endemic countries in the implementation of the projects. The portion of the TDR operations budget obligated directly to these countries has risen from 29 per cent in 1977 to 55.4 per cent in 1979. All funds allocated for research capability strengthening go to institutions and scientists in developing countries, and approximately 50 per cent of research and development projects take place in these institutions. In addition, the great bulk of research and development work supported in developed countries involves close collaboration with developing country institutions or the training of their scientists. Following is a brief description of some of the main scientific highlights and results achieved to date.

Malaria

5. The main objectives of the work in malaria are: the improvement of existing drugs and the development and application of new ones; the development of vaccines and improvement of immuno-diagnostic tests; and improvement of methods of malaria control. High priority is being given to the clinical development of mefloquine, a promising new antimalarial drug which is effective against chloroquine-resistant strains of the parasite. Phase I and II clinical trials of mefloquine have been initiated in Latin America and Africa, and a Phase II dose-finding study is under way in South-East Asia. Progress has been made towards the development of sustained release formulations of antimalarial drugs and it is hoped that one such formulation will be available for preclinical testing in the very near future. In the area of immunology, immunodiagnostic tests have been improved, and a sensitive test is being developed for the detection of low levels of infection by the detection of malaria antigens in blood. In the area of malaria control, extensive training is being supported, and a large project on the epidemiology and control of malaria in different ecological areas in West Africa is providing important new data for use in formulating control strategies. A global effort, involving 20 countries, includes studies on alternative drug regimes, and kits for *in vitro* sensitivity testing are being produced and distributed widely.

Schistosomiasis

6. The objectives of the work in schistosomiasis are to: improve current methods of schistosomiasis control; develop or make accessible better drugs than those currently available; and study the immune responses to improve understanding of the mechanisms of the pathological processes and possibly lead to the development of a vaccine. Research is in progress on epidemiology and snail control, chemotherapy and biochemistry, immunology and basic sciences, and field research. The pharmaceutical industry is interested in the development of schistosomicidal drugs and TDR has continued to support this effort, especially through clinical

evaluation of promising new agents. In collaboration with industry, clinical trials have been carried out on a promising new drug, praziquantel, and the Special Programme is now collaborating in the field trials. In addition, the modes of action of various drugs and their metabolic pathways are being clarified, and it appears that the effectiveness of some antischistosomal drugs is dependent upon the immune response of the host. Antigenic materials are being purified for immuno-diagnostic tests and possible vaccine development.

Filariasis

7. The Scientific Working Group on Filariasis is active in three main areas: chemotherapy; immunology and pathology; and epidemiology, field research and vectors. The objectives are to: improve the use of existing filaricides and to find new ones; find means of reducing the inflammatory reactions to filarial parasites in man; identify filarial antigens for serodiagnostic tests and for possible vaccine development; and improve control of transmission in problem situations through the understanding of the vector and human components of filarial infections. Chemotherapy activities aim to improve the treatment of onchocerciasis; find and develop new drugs effective against the adult worms; and determine practical dosage schedules for large-scale treatment of lymphatic filariasis. In the search for new filaricides more than 970 compounds have been screened at the primary level, and a secondary Onchocerca screen in cattle has been developed. Mebendazole and flubendazole appear to be promising leads. Investigations into the causes and prevention of inflammatory reactions to the death of microfilariae are in progress in animal models and in man. Efforts are being made to develop in vitro and in vivo culture systems as a source of parasite antigens for improved serodiagnostic tests, and for the development of possible vaccines. Several Simulium and Mansonia vector projects have commenced. Isoenzyme studies under way indicate distinguishing features in filarial parasites that may have edpidemiological significance.

African trypanosomiasis

8. This component of the Programme deals with epidemiology, chemotherapy and immunology/pathology. The objectives are to: improve understanding of the epidemiology of African trypanosomiasis; develop simple diagnostic tests; develop new chemotherapeutic agents; improve clinical management of patients and define standard procedures of treatment; and improve tsetse fly control. A new diagnostic test card for trypanosomiasis has been developed that provides on-the-spot results in less than five minutes. The initial promising results have been readied for a major field test in West Africa. If successful, this test can be applied widely in the field by auxiliary health personnel. An appropriate combination of antigens is being sought to prepare a similar card for Trypanosoma brucei rhodesiense. A new technique for detecting low levels of parasitaemia has been developed, and important information about the effects of aerial spraying of insecticides in the control of the tsetse fly has been obtained. In addition, a major epidemiological study of T.b. rhodesiense has been initiated in north-eastern Zambia and an illustrated manual for autopsy procedures has been written in French and English and distributed to six medical facilities participating in collaborative clinical and pathological studies.

Chagas' Disease

9. Research approaches to the treatment and control of Chagas' Disease include epidemiology, pathology, and vector control; parasitology, biochemistry, and drug development; and immunology and immuno-pathology. Among the early results is a standard protocol to carry out cross-sectional and longitudinal, epidemiological studies. This is now being applied in Bolivia, Chile, Colombia, Mexico, Panama and Peru. Promising data have resulted from studies on new organophosphorus insecticides, and antitriatomid building materials in Argentina and Brazil and from a community participation-based programme for housing improvement and vector control in a rural area in Brazil. Potential trypanocides are being screened and a specific enzyme inhibitor of T. cruzi has been identified which may yield new leads for drug development. A serum reference bank has been established to develop standardized immuno-diagnostic tests and diagnostic criteria and possible murine and primate animal models are being studied.

Leishmaniasis

10. The objectives of the three research approaches in this area are: to obtain precise information on the geographical distribution, incidence, and prevalence of the human disease, and to design better methods for control; to define optimal treatment schedules using currently available drugs and develop new therapeutic compounds; and to develop better immuno-diagnostic tests and a reference serum bank. Development of a vaccine is a long-term objective. A modest drug development programme has commenced. Epidemiological projects and studies on phlebotomine sandflies have been initiated in several countries. Research is in progress on experimental immunization, and mechanisms of host resistance, and certain leishmanial antigens.

Leprosy

11. Research in the leprosy component is carried out in two main areas, namely, immunology and chemotherapy. In 1979 this component was subjected to an independent in-depth evaluation, with the conclusion that the projects supported have been highly productive. Work in the immunology of leprosy has reached a stage where the development of an effective vaccine against leprosy is a distinct possibility. Preliminary studies are being planned to obtain information which will enable a potential vaccine to be evaluated. In the area of chemotherapy the objectives are to find better ways to use existing drugs, develop new drugs, and assess national needs for new chemotherapeutic approaches. Clinical trials of combinations of drugs have been initiated in India and West Africa, using a standardized protocol. Drug development projects are under way, including the synthesis, screening and study of modes of action of compounds. Survey of prevalence of dapsone resistance are also in progress.

Trans-disease aspects

12. In addition to the above work on the individual diseases, the Programme involves research and development, training, information exchange and other activities in four areas dealing with problems applicable to all the diseases. These areas are: fundamental biomedical research aimed at developing new approaches for diagnosis, therapy,

prevention and control; vector biology and control; epidemiology; and social and economic research. One result achieved has been familiarization of scientists, working in the basic biomedical sciences, with the goals of the TDR Programme, and the provision of information regarding relevant progress in biomedical science to those working on specific target diseases. In the area of vector biology and control the most significant progress thus far has been the promising results obtained with a spore-forming bacterium, serotype H-14 of Bacillus thuringiensis, in the biological control of mosquito and blackfly larvae. Epidemiological training is being improved, and protocols for analytical epidemiological studies on malaria, schistosomiasis and trypanosomiasis are under development. Social and economic research is contributing to the development of guidelines for resource allocation decisions.

Research capability strengthening

13. The concept of the Special Programme is based upon the greatest possible participation of the affected tropical countries. It will be through their efforts that the diseases will ultimately be brought under control. They are involved in research at all levels, not solely in those activities which of necessity must take place in endemic regions, as for example, epidemiological and operational research and the evaluation of new drugs, vaccines and diagnostic tests. The Programme therefore stimulates these countries to assume an ever increasing role in the research required to identify, analyze and solve their health problems, and provides assistance to enable them to fulfill this responsibility, through institutional support and a programme of research training to complement it. In 1979, 75 research training grants, 7 re-entry grants, and 15 visiting scientists grants were awarded, and 10 group training activities were supported. In addition, 19 institutions received various types of support ranging from one-time capital grants to long-term programmes of support. All such awards are made to institutions and trainees of the developing endemic countries, and all research strengthening activities are developed in close collaboration with national authorities in the context of their needs and resources. The ultimate objective is to establish a network of collaborating institutions in tropical endemic countries.

14. While the accomplishments of the Special Programme to date are impressive, it must be recognized that the work has barely begun, and that the eradication of the six target diseases will be a long-term endeavour of perhaps 15 to 20 years. The strengthening of the research capabilities of the affected countries can be achieved only through sustained co-operation with the national authorities, and development and application of new and improved technologies for the control of the diseases will also take many years. The co-sponsors of the Programme and Co-operating Governments and Agencies understand and accept these facts. It is recognized that the achievement of the objectives established for the Programme, although costly, will contribute substantially to human well-being and the possibility of health for all by the end of the century. The Administrator attaches the highest importance to the attainment of that goal, and considers that UNDP should continue to support the Special Programme during the third Indicative Planning Figure (IPF) cycle. UNDP support will continue to be provided to the Programme as a whole, without being earmarked for any particular component of the Programme. It should be noted that the contribution herewith recommended will commence only in January 1983, since the present allocation approved by the Council at its January 1978 meetings was for the five-year period 1978-1982 inclusive. The recommendation is being submitted to the

Council at its present session because a system of biennial budgeting has recently been adopted by the co-operating parties, and UNDP, as a principal co-sponsor, should be legally enabled to pledge for the years 1982 and 1983 at the next pledging session, which will take place towards the end of 1981.

15. The components of the proposed UNDP inputs are as follows:[a/]

Subcontracts	$7 507 300
Miscellaneous	60 000
	$7 567 300

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a/ Since UNDP is a co-sponsor of the TDR Programme, no agency overhead costs will be charged to this project which forms part of the UNDP/WHO/World Bank Special Programme for Research and Training in Tropical Diseases.

III. Recommendation

16. The Administrator recommends that the Governing Council:

(a) Approve UNDP assistance to this project; and

(b) Authorize the Administrator to make the appropriate arrangements with the Executing Agencies for the execution of this project.

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